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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,894	09/22/2004	Ajita Bhat	P51328	9704
20462 7590 07/19/2007 SMITHKLINE BEECHAM CORPORATION CORPORATE INTELLECTUAL PROPERTY-US, UW2220 P. O. BOX 1539 KING OF PRUSSIA, PA 19406-0939			EXAMINER TUCKER, ZACHARY C	
			ART UNIT 1624	PAPER NUMBER
			MAIL DATE 07/19/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/508,894

Applicant(s)

BHAT ET AL.

Examiner

Zachary C. Tucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49-67, 70, 71 and 92-107 is/are pending in the application.
- 4a) Of the above claim(s) 65, 67, 70, 92-104, 106 and 107 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 49-64, 66 and 71 is/are rejected.
- 7) ☒ Claim(s) 105 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 25May07.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

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**Response to Amendment
~and~
Status of Lack of Unity of Invention**

As requested by applicants in the response filed 7 May 2007 (hereinafter "present amendment") which is in reply to the Office action mailed 5 February 2007 (hereinafter "previous Office action"), instant claims 49, 71 and 102 have been amended, while claims 68, 69 and 72 have been cancelled. New claims 105-107, drawn to series of named compounds, have been added. (It is noted that new claims 106 and 107 depend from claim 49, while new claim 105 is an independent claim.)

Applicants are advised, that since there are such a great many compounds specified in instant claim 105, each of which is individually named, there is likelihood for some deficiencies being present in that claim. Applicants are urged to carefully proofread the claim for typographical errors, and inspect it for the inclusion of any compounds that are not described by Formula I in instant claim 49. Claim 105 is an independent claim, so it is not technically necessary for compounds named in that claim to have antecedent basis in claim 49. However, because compounds of instant claim 105 must be within the scope of Group I as set forth in the finding of Lack of Unit of Invention which is presently in effect, they must in fact be embraced by Formula (I). The finding of Lack of Unity of Invention identified Group I as "drawn to chemical compounds of the Formula (I), and a pharmaceutical composition comprising the same." So, the subject matter elected for examination is Formula I compounds. Compounds according to new claim 105, in order to be part of the subject matter elected by applicants for examination, therefore, must be within the scope of generic claim 49, where Formula I is defined, even though claim 105 is an independent claim itself. The compound indicated by applicants as the elected species

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for examination, the compound of Example #10, appears as the 10th named compound in claim 105.

The elected species for examination is not, however, named in new claims 106 and 107, so those two claims, in addition to claims 65, 67, and 70 indicated as such in the previous Office action, are withdrawn from consideration at this time.

Since the present amendment and reply does not place the claims of Group I in condition for allowance (Group I now consists of claims 49-67, 70, 71 and 105-107), the claims of Group II (claims 92-104) are not eligible for rejoinder. Group I was elected without traverse in applicants' reply to the finding of Lack of Unity of Invention filed 28 November 2006.

In total, claims 65, 67, 70, 92-104, 106 and 107 are withdrawn from consideration at this time, either as being drawn to an invention nonelected without traverse, or as not being readable on the elected species. At such time that the claims of Group I are in allowable form, Group II claims will be eligible for rejoinder. The finding of Lack of Unity of Invention will be withdrawn when rejoinder occurs. Applicants are advised that the claims in Group II are likely to be found noncompliant with the first paragraph of 35 U.S.C. 112 upon rejoinder, for reasons explained in the previous Office action, pages 11 and 12.

The present amendment has overcome the rejections set forth in the previous Office action, so, in accordance with "Markush practice" as explained in MPEP 803.02, the prior art search has been broadened and expanded. Only compounds of Formula (I) wherein

Status of Claim Rejections - 35 USC § 112

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In the previous Office action, claims 49-66, 68, 69, 71 and 72 were rejected under 35 U.S.C. 112, first paragraph, for lack of a disclosure enabling the production of the full scope of the claimed solvates of Formula Compounds.

Rejection of claims 68, 69 and 72 is moot due to those claims having been cancelled.

Rejection of claims 49-66 and 71 is hereby withdrawn in view of the present amendment to claim 49, which deletes reference to "solvate thereof," in favor of the "or a hydrate thereof" language proposed by the examiner. Hydrates of Formula (I) compounds of the invention could be prepared without undue experimentation.

Claims 49-66, 71 and 72 were rejected under 35 U.S.C. 112, second paragraph, in the previous Office action, for indefiniteness, because two variables were not defined in Formula (I). "Ar" and "Het" did not have definitions. Because the present amendment to claim 49 has introduced definitions for "Ar" and "Het" the rejection of instant claims 49-66 and 71 under 35 U.S.C. 112, second paragraph, for indefiniteness, is hereby withdrawn. The newly added definition for "Het" is problematic, however, and a new rejection under 35 U.S.C. 112, second paragraph, is necessary (*vide infra*).

Claims 71 and 72 were deemed to be further indefinite, in addition to the fact that not all variables were defined, because the pharmaceutical composition specified in those claims lacked the recitation of some diluent, excipient or carrier. As such, claims 71 and 72, although being drafted as "a pharmaceutical composition comprising [a compound of the present invention]," the claim could read on a composition comprising the inventive compounds in combination with other substances (including pharmaceutical composition diluents, excipients or carriers), or the claim could be interpreted as reading on the pure compound, the compound *per se*, in other words. If the claims were intended to be

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inclusive of the latter interpretation, then they were potentially duplicating the subject matter claimed in claim 49.

Claim 72 has been cancelled, rendering any rejection of that claim moot.

In view of the present amendment to claim 71, adding a pharmaceutically acceptable carrier or diluent, the rejection of claim 71 under 35 U.S.C. 112, second paragraph is hereby withdrawn.

Claims 68 and 69 were rejected under 35 U.S.C. 112, second paragraph in the previous Office action for being further indefinite, in addition to the reason that they depended from indefinite claim 49, because the manner in which the series of compound names was set out created uncertainty as to what the scope of the claims was. Claim 69 depended from claim 68, yet the use of commas and semicolons as alternative punctuations for separating compound names from one another was inconsistent between claim 68, and claim 69, which depended from claim 68.

This inconsistency with the use of commas versus semicolons rendered the claims' scope indefinite, at least in part, because was not clear if some of the names with commas appearing between were not actually intended to be one long chemical name.

Claim 69, lastly, was further indefinite, in addition to the reasons described in the preceding, because the limitation "or racemate mixture thereof" was recited in the latter part of the claim. This is contradictory in general to the subject matter specified in the claim, because many of the named compounds are those in single-isomer form.

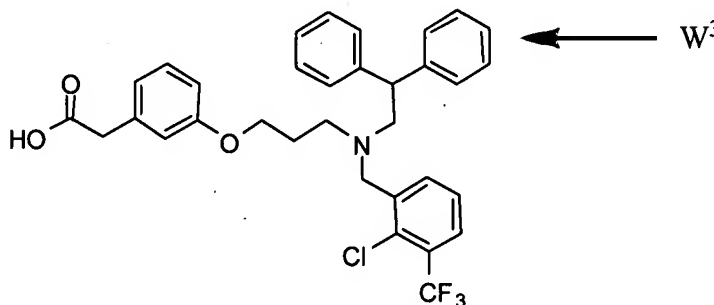
Claims 68 and 69 have both been cancelled by the present amendment, so the rejections of those two claims are effectively moot.

Status of Claim Rejections - 35 USC § 102

In the previous Office action, claims 49-64, 66, 68, 71 and 72 were rejected for being anticipated by United States Patent Application Publication 2004/0072868 (Collins et al). The Collins et al publication is prior art against the instant application under 35 U.S.C. 102(e), due to its domestic priority claim to the filing date of provisional U.S. patent application serial no. 60/233,144, 18 September 2000, which was before the instant application's domestic priority claim to the filing date of provisional U.S. application no. 60/368,425, 27 March 2002.

As the basis of the anticipation rejection of the instant claims over Collins et al, the examiner noted a compound named in section [0121] of the specification, on page 7, named 2-(3-[3-[[2-chloro-3-(trifluoromethyl)benzyl](2,2-diphenylethyl)amino]propoxy]-phenyl)acetic acid. The synthesis of this compound is taught in Example #18, found on page 19. It is specified as a particular species in claim 68 of the application publication.

The molecular structure of the compound of Example #18 in the Collins et al publication is represented by the diagram shown:



Applicants traverse the rejection, on grounds that that W^3 , which was identified as being an aryl group in the rejection, may not be an aryl group.

Upon reconsideration of the rejection, the examiner agrees with applicants' argument – W^3 is not permitted to be aryl. More importantly, the reference compound from Collins et al is not within the scope of the present claims, because the proviso

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language specifies that W^3 may not be -H when the other variables have the identities that they have in the reference compound. Therefore, the rejection under 35 U.S.C. 102(e) based on Collins et al, as stated in the previous Office action, is hereby withdrawn.

Status of Obviousness-Type Double Patenting

In the previous Office action, claims 49, 71 and 72 were provisionally rejected under the judicially-created doctrine of Obviousness-Type Double Patenting, as being unpatentable over claim 22 of copending Application No. 10/ 508,791.

Applicants traversed the rejection in the present amendment and reply. In view of applicants' arguments, the rejection is hereby withdrawn. The carboxamide group in the structure diagram specified in claim 22 of the copending application is reversed as compared with the carboxamide group formed by instant Formula (I) when the variables have the identities stated in the rejection, so compounds of the copending application are not actually within the scope of the instant claims.

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

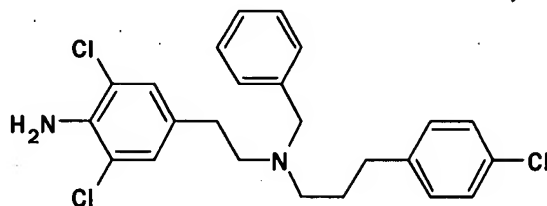
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-64,66 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The latter part of claim 49 includes a lengthy list of named compounds that are limitations of a "provided that the compound is not" proviso. One such named compound – the seventh in the list – whose name and structure diagram are shown below, cannot be

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constructed from Formula I. It is therefore not necessary to specify that claim 49 does not include this compound.



4-(2-(benzyl(3-(4-chlorophenyl)propyl)amino)ethyl)-2,6-dichloroaniline

This compound is not embraced by Formula I because "Y" is not present.

Because the limitation "provided that the compound is not," appearing in instant claim 49, followed by a list of named compounds that includes at least one compound which is definitely not embraced by Formula (I) introduces ambiguity into the meaning of the claim, claim 49 is rejected as indefinite. There are many compounds named in the provisional statement found in claim 49, so the examiner urges applicants to study this list of compounds and delete any others which cannot be formed from Formula I.

Claim 49 is further indefinite, in addition to the reason given above, because the newly added definition for variable "Het" is ambiguous. It appears that "Het" is limited only to *tricyclic* ring groups having 5- to 7-membered, 7- to 10-membered or 11- to 18-membered heterocyclic rings, due to the manner in which the definition is phrased. At page 11 of the instant specification, "Het" is defined as a "5- to 7-membered monocyclic, 7- to 10-membered bicyclic, or 11- to 18-membered tricyclic heterocyclic ring group." The instant claims have been examined as though "Het" is as defined on page 11 of the instant specification. Correction is necessary.

Claims 55 and 66 are further indefinite, in addition to being indefinite for the reasons explained in the preceding, because the limitation, "or X an an adjacent R³, taken together with the atoms to which they are bonded, form an alkylenedioxy moiety," which is

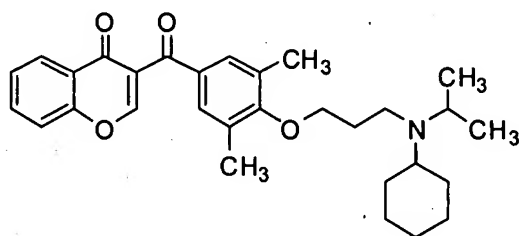
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recited in both claims, lacks antecedent basis in independent claim 49. In claim 49, the independent claim, neither the definition for "X" or "R³" contemplates this arrangement.

New Claim Rejections - 35 USC § 102

Claims 49-52, 54, 55, 57, 59, 62, 64 and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,220,645 (Chibret).

Chibret discloses chromone derivatives and a pharmaceutical composition comprised thereof. In Table III, which appears in columns 15 and 16, a compound having this structure:



It is embraced by instant claims 49-52, 54, 55, 57, 59, 62 and 64 where $p=0$; X is $-\text{COR}^{13}$ with R^{13} being $-\text{C}_0\text{-C}_6$ alkyl-Het - alkyl is " C_0 " and "Het" is a 10-membered bicyclic heterocyclic ring system; Z is $-\text{CH=}$; $k=2$; both R^3 are $\text{C}_1\text{-C}_6$ alkyl (methyl); Y is $-\text{O-}$; $m=0$; W^1 is $\text{C}_1\text{-C}_6$ alkyl (methyl); W^2 is $\text{C}_1\text{-C}_6$ alkyl (methyl); W^3 is $-\text{H}$; $t=0$; $q=0$; Q is $\text{C}_3\text{-C}_8$ cycloalkyl (cyclohexyl). Tablets for human use, comprising the compounds, are taught in Example X.

Claims 49-62, 66 and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/18723 (Sikorski et al).

An abstract of the (lengthy, in excess of 200 pages) Sikorski et al publication, as published by Chemical Abstracts Service, obtained from the "CAPLUS" database on the STN technical information service, is submitted with this Office action for applicants' review.

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Sikorski et al discloses arylaminoalkanols, which are taught to have utility as cholesteryl ester transfer protein inhibitors. Many different genera of compounds are disclosed. Compounds which anticipate subject matter of the instant claims are diagrammed in the abstract. The first structure diagram shown corresponds to a compound according to instant claims 49-62, 66, and to a pharmaceutical composition according to instant claim 71, wherein X is halo (chloro); p=0; Z is -CH=; k=1; R³ is C₁-C₆ alkyl (methyl); Y is -O-; t=0; q=0; Q is Ar (phenyl), substituted with an alkyl which in turn is substituted with 3 halogen atoms (trifluoromethyl); m=0; W¹ is C₁-C₆ alkyl (ethyl), substituted with three halogens and one group of the formula C₀-C₆ alkyl-OR¹⁰ with R¹⁰ being -H and "C₀-C₆" being a bond, yielding -OH - a 2,2,2-trifluoro-1-hydroxy-ethyl group; W² and W³ are both -H; all of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹ are -H.

The other compounds whose structures are diagrammed in the abstract are within the scope of the instant claims as well, but the substituents on the phenyl ring corresponding to the "Q" ring of the instant claims is different in these other compounds.

It must be noted that the compounds disclosed in the Sikorski et al abstract also would anticipate the embodiment of the instant claims wherein "X" and "R³" are transposed - in other words, "X" could be alkyl and "R³" instead could be halo, with "k" maintaining a value of 1.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,220,645 (Chibret).

At the time the invention was made, a compound according to instant claim 53 would have been obvious to the skilled chemist, given the teaching of the Chibret patent. The limitation on the value of variable "k" posed by claim 53 does not serve to patentably distinguish the subject matter thereof from the teaching of Chibret. According to Chibret (columns 3 and 4), the substituents R₁ and R₂ on the phenyl ring, which correspond to the variable R³ in instant claim 49, may either be hydrogen or lower alkyl. Thus, a derivative of the compound disclosed in the Chibret patent, cited in the rejection of claims 49-52, 54, 55, 57, 59, 62 and 64 under 35 U.S.C. 102(b), wherein one or both of the methyl groups on the phenyl ring are hydrogen would clearly be an obvious modification of the exemplified compounds disclosed by Chibret. Such a compound would correspond to instant claim 53, wherein the subscript "k" is 0 or 1. The motivation to make such a compound would arise from, as taught by Chibret, a desire to produce drugs that act as antiarrhythmic or anti-angina agents (examples V through VIII in the patent describe the pharmacological activity of the compounds).

Information Disclosure Statement

An Information Disclosure Statement filed 25 May 2007 has been considered by the examiner. Initialed, signed and dated forms PTO-1449 accompanying that Information Disclosure Statement are provided with this Office action. The last item cited on page two of the PTO-1449 has been "lined through" because it is a copy of the same Office action to which the present amendment is in reply.

Conclusion

Because of the new rejections under 35 U.S.C. 112, second paragraph, which were not actually necessitated by applicants' present amendment, this Office action is non-final.

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Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 9:00am to 5:00pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

A handwritten signature in black ink, appearing to read 'Zachary C. Tucker', with a stylized flourish at the end.

ZACHARY C. TUCKER
PRIMARY EXAMINER